This educational material is part of the marketing authorization and is approved by the executive directorate of Pharmacovigilance, at SFDA.

Important Risk Minimization Information for Healthcare Professionals.

Drug Product: Methotrexate Venus

(Methotrexate Injection USP

50 mg/2ml)

This Healthcare provider guide has been prepared to increase the awareness of healthcare professionals (HCPs) on the risk of medication errors/overdose, dispensing and prescription with methotrexate Venus.

Methotrexate is indicated in the treatment of neoplastic disease, such as trophoblastic neoplasms and leukaemia, and the symptomatic treatment of severe recalcitrant disabling psoriasis which is not adequately responsive to other forms of therapy.

This document should be read in conjunction with the Summary of Product Characteristics (SmPC) for full prescribing information and other relevant clinical guidance on the prescribing and dispensing of methotrexate.

Methotrexate is a cytotoxic agent, daily administration of a weekly dose can lead to overdose and to serious adverse outcomes, including death. Elderly patients are especially susceptible to serious toxicities. Despite risk minimisation measures are already in place, errors continue to be reported.

It is important to note that the patient doctor will work out the correct dose of methotrexate injection for patient and how often it must be given since the dose of medicine given.

Purpose of this educational guide

• To inform about the potential for fatal overdose due to medication errors and how to minimize.

• To highlight the need to inform patients with autoimmune diseases and others about once weekly dosing.

• To provide information on the importance of writing prescriptions with clear instructions about dosing, and not to use abbreviations.

• To remind pharmacists to counsel the patient about accidental overdosing.

It is recognised that medication errors can sometimes happen despite appropriate prescribing and patient/carer instruction. Therefore this guide also describes the risks and what to do in the event of a medication error/overdosing.

How to minimize medication error

For the treatment of cancer, the frequency depends on the regimen and can require daily administration of methotrexate but for ***Patients with autoimmune diseases must be told that methotrexate must only be taken once a week.***

- Patients with autoimmune diseases should be advised to write the treatment day on their **Patient alert Card**, and to carry it with them.
- It is important to discuss signs and symptoms of adverse reactions with the patient, which will enable them to recognise possible events of overdose.
- Do not use abbreviations or shorthand.

- Specify the indication, strength and dose (in mg) within the prescription.
- Verify dose and administration instructions for methotrexate before dosing.
- Methotrexate is contraindicated in pregnancy and lactating women.
- **Only the Methotrexate 50 mg/2 ml presentation should be used for the intrathecal route of administration to prevent accidental overdose**.
- That greater doses or higher frequencies are associated with an increased risk of serious adverse events, including death.
- If they do make a mistake to record and report to their doctor or pharmacist what they have taken and when.

Dispensing requirements

- On dispensing the pharmacist should transcribe the defined day of the week for intake for patients with autoimmune disease.
- Onto the **patient alert card** provided within the pack/ on the outer packaging. The pharmacist should show the patient card to the patient/carer, reiterate the once weekly dosing
- Schedule and the other elements described on the **patient alert card**.
- Follow-up visits

Risks associated with overdose

In post marketing experience with methotrexate, reports of overdose that indicate accidental daily administration instead of weekly is associated with a risk of serious harm. Symptoms commonly reported with overdose are haematological and gastrointestinal reactions. For example, leukopenia, thrombocytopenia, anaemia, pancytopenia, bone marrow suppression, mucositis, stomatitis, oral ulceration, nausea, vomiting, gastrointestinal ulceration and gastrointestinal bleeding.

Therapeutic management of overdose (SmPC Section 4.9)

This medicine will be given to you in a hospital, under the supervision of a doctor. It is unlikely that you will be given too much or too little However if the patient is not already in a clinical setting then they should immediately go to their local Emergency Department bringing their medication, including the packaging. On arrival they should present their medication and tell the reception/registration desk that they are taking methotrexate and have been instructed by the prescriber that immediate treatment is required in the event of an overdose.

Calcium folinate (calcium leucovorin) is a potent agent for neutralizing the immediate toxic effects of methotrexate on the haematopoietic system. Where large doses or overdoses are given, calcium folinate may be administered by intravenous infusion in doses up to 75 mg within 12 hours, followed

by 12 mg intramuscularly every 6 hours for 4 doses. Where average doses of methotrexate appear to have an adverse effect 6-12 mg of calcium folinate may be given intramuscularly every 6 hours for 4 doses. In general, where over dosage is suspected, the dose of calcium folinate should be equal to or higher than, the offending dose of methotrexate and should be administered as soon as possible; preferably within the first hour and certainly within 4 hours after which it may not be effective. Effective clearance of methotrexate is reported to be achieved with acute intermittent haemodialysis using a high-flux dialyser.

Reporting of Adverse Reactions:

Mesned Pharma Consult Center Pharmacovigilance Department on behalf of Venus:

E-mail: mpv@mesned.com

The National Pharmacovigilance Centre (NPC) Saudi Food and Drug Authority (SFDA):

SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/